Remarks/ Arguments

This Amendment is submitted in response to the office action mailed June 11, 2009, in connection with the above-identified application (hereinafter, the "Office Action"). The Office Action provided a three-month shortened statutory period in which to respond, ending on September 11, 2009. Submitted herewith is a Petition for a Two-Month Extension of Time extending the due date to November 11, 2009. Accordingly, this Amendment is timely submitted.

Claims 1 through 47 are currently pending. Applicants have amended Claims 1, 4, 8, 12, 18, 23, 29, 34 and 39 to highlight that the drug polymeric solution remains a free flowing liquid upon parenteral administration to a warm blooded animal and at temperatures between 35 and 42°C and cancelled Claims 44-47, which when considered with the following remarks, is deemed to place the present application in condition for allowance. Support for the amendment to Claims 1, 4, 8, 12, 18, 23, 29, 34 and 39 may be found throughout the specification including, for example in lines 9-12 of page 1, lines 5-7 of page 6, lines 5-7 and 11-14 of page 7 and lines 3-7 of page 9 of the original description and the original claims of the filed application. Accordingly, these claims are now in condition for allowance.

Applicants respectfully submit that the foregoing amendments to the claims and specification do not add any new matter.

Rejection under 35 U.S.C. §112

Claims 1-47 are rejected under 35 U.S.C. §112, first paragraph as allegedly failing to comply with the written description requirement based upon new matter rejections. Applicants respectfully submit that the pending claims as amended do not include new matter and satisfy the written description requirement.

Claims 1, 3, 8, 12, 18 and 23 are rejected under 35 U.S.C. §112, first paragraph for allegedly including new subject matter in which the polymeric composition remains free flowing at all temperatures. Based upon the Examiner's comments, it is believed that the Office Action mistakenly referred to dependent claim 3 (which depends from independent claim 1) instead of independent claim 4. Applicants have responded in accordance with this interpretation but request notification if this interpretation is erroneous.

Applicants have amended Claims 1, 4, 8, 12, 18, 23, 29, 34 and 39 of the present application to specify that the polymeric composition remains free flowing upon parenteral

administration to a warm blooded animal and at temperatures between 35 and 42°C. Support for this amendment is found throughout the original application including, for example, paragraph 1 on page 6 of the original filed specification or paragraph 0017 of the published application.

Claims 44 and 46 are rejected under 35 U.S.C. §112, first paragraph since applicants allegedly failed to identify support for the limitations in the new claims 44 and 46 that a polymer comprises 52% A-block and 48% B-block. Further, claims 45 and 47 are rejected under 35 U.S.C. §112, first paragraph for allegedly including new subject matter by identifying the single molecular weight point of 3099 Dalton for the polymer.

Applicants have cancelled Claims 44-47 from consideration in the present application. Applicants reserve the right to pursue the subject matter of Claims 44-47 in a future related patent application.

Claims 9, 14, 24, 30, 35 and 40 are rejected under 35 U.S.C. §112, first paragraph for allegedly including new subject matter by identifying the block co-polymer concentration of between 10-30%. Applicants respectfully submit that amended Claims 9, 14, 24, 30, 35 and 40 satisfy the written description requirement and do not include new matter. Support for the limitation "wherein said block copolymer concentration is between about 10 to 30% by weight of said polymer solution" of Claims 9, 14, 24, 30, 35 and 40 is found in the original filed application including, for example, the third paragraph (lines 15-21) on page 11 of the original filed specification or paragraph 0042 of the published application.

Claims 1-43 are rejected under 35 U.S.C §112, second paragraph, as allegedly being indefinite. Specifically, Claims 1, 3, 8, 12, 18 and 23 are allegedly ambiguous regarding whether the polymeric composition is "free flowing upon administration" requires it to be free flowing before or after it enters the physiological system. The Examiner has stated that the claims are examined for the composition that is free flowing before it actually enters the body (Office Action, paragraphs 10-11).

Applicants respectfully submit that the term "upon administration" as used in Claims 1, 3, 8, 12, 18, 23 satisfy the definiteness requirement of 35 U.S.C §112, second paragraph. During patent examination, the pending claims must be "given their broadest reasonable interpretation consistent with the specification". MPEP §2111. "The Patent and Trademark

Office determines the scope of claims in patent applications not solely on the basis of the claim language, but upon giving claims their broadest reasonable construction 'in light of the specification as it would be interpreted by one of ordinary skill in the art'." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1316 (Fed. Cir. 2005).

Applicants respectfully submit that one of ordinary skill would readily understand the claim term "upon administration" as used in amended Claims 1, 3, 8, 12, 18 and 23 to refer to the moment when the pharmaceutical composition enters the physiological system of a warm-blooded mammal and immediately thereafter. In the original filed application, the specification emphasizes that the "triblock copolymers of the present invention...form solutions in aqueous environments at body temperature". The original filed specification further emphasizes that the drug polymer solution of the present invention is "free flowing at temperatures relevant for administration" and that physiologically relevant temperatures for intravenous administration are 35-42°C. (lines 4-7 and lines 11-14 of page 7.) The original filed specification further emphasizes that the "drug may be delivered to a human or any other warm blooded animal much more effectively as an aqueous solution with the biodegradable triblock copolymers of the present invention". (Lines 3-5 of page 9.) Based upon these excerpts, one of ordinary skill would understand that the claim limitation "upon administration" refers to the drug polymer solution when the pharmaceutical composition enters the physiological system of a warm-blooded mammal and immediately thereafter.

In addition, Applicants submit that one of ordinary skill in the art would interpret the claim term "upon administration" in context of those statements distinguishing the present invention from prior methods in the original specification. The specification clearly states that U.S. Patent Nos. 6,004,573; 6,117,949 and 6,201,072 are distinguishable from the present invention since these prior patents "possess reverse thermal gelation properties wherein the sol/gel transition temperature is generally lower than a temperature required for IV delivery purposes of between at least 35-42°C" (lines 15-17 of page 4) whereas the present invention is a "free flowing solution" at the same physiological temperatures (lines 20-24 of page 4 and lines 1-7 and 11-14 of page 7.) One of ordinary skill would understand that the claim limitation "upon administration" refers to the drug polymer solution when the drug enters the physiological system of a warm-blooded mammal and immediately thereafter.

In view of the foregoing amendments and remarks, Applicants respectfully submit that Claims 1 to 47 of the present application properly comply with the written description and definiteness requirements of 35 U.S.C. §112, first and second paragraphs. Applicants

request that Claims 1 to 47 of the present application be reconsidered for allowance and the Examiner's rejection be withdrawn.

Rejections under 35 U.S.C. §§ 102(b) and 103

Claims 1-47 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by or, in the alternative, under 35 U.S.C. §103(a) as obvious over U.S. Patent No. 6,004,573 to Rathi et al (hereinafter "Rathi et al").

Pursuant to 35 U.S.C. §102, "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987), M.P.E.P. §2131. The identical invention must be shown in as complete detail as contained in ...the claims." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236 (Fed. Cir. 1989).

Applicants respectfully submit that amended Claims 1-43 are patentable under 35 U.S.C. §102(b) over Rathi et al. Claims 44-47 have been cancelled. Upon careful analysis, it is clear that Rathi et al does not expressly or inherently describe each and every limitation of amended Claims 1-43. Applicants incorporate by reference their detailed arguments above explaining the basis for interpreting the claim term "upon administration" to refer to the drug polymer solution when the drug enters the physiological system of a warm-blooded mammal and immediately thereafter.

The present invention of amended claims 1-43 is directed to a specific drug polymer solution comprising a biodegradable ABA-type or BAB-type block copolymer comprising: (1) 50.1 to 65% by weight of a biodegradable, hydrophobic A polymer block comprising a biodegradable polyester, and (2) 35 to 49.9% by weight of a hydrophilic B polymer block comprising PEG, wherein the block copolymer has a weight averaged molecular weight of between 1500 and 3099 Daltons. In addition, the polymeric composition when formed as an aqueous polymer solution remains a free flowing liquid upon parenteral administration to a warm blooded animal and at temperatures between 35 and 42°C.

The Examiner incorrectly states that the claim limitation "free flowing liquid at body temperatures" recited in claims 1, 4, 8, 12, 18, 23, 29, 34 and 39 is the property of the Rathi et al formulation composition. In contrast to the present invention, Rathi et al expressly teaches a specific polymeric solution having a high molecular weight of 3100 to 4500 Daltons which possesses reverse thermal gelation properties at or below body temperature

of a warm-blooded animal. (See, e.g., Rathi et al, abstract; Column 1, lines 16-21; Column 4, lines 56-61, Column 5, lines 24-52, Column 6, lines 36-39, and Column 10, lines 26-32.) Rathi et al expressly teaches that its polymeric composition spontaneously forms a gel at or below the body temperature of a warm blooded animal which differs from the Examiner's assertion.

The Examiner further incorrectly states that Rathi et al discloses an ABA-type block copolymer which "gels at body temperature, which is 37°C (abstract and column 1, lines 19-21) and this means that between 35°C and 36.999°C, the ABA-type polymeric composition of Rathi is a liquid. In context, the cited portions of Rathi et al limitedly disclose that their compositions include "a select subset of such block copolymers" having a gelation temperature "at or below body temperature of a warm-blooded animal" which, "when the temperature is raised to about body temperature (typically 37°C for humans), spontaneously interacts to form solid hydrogels (i.e., gels)". (See Rathi et al, abstract and column 1, lines 15-23.) These cited portions of Rathi et al do not expressly or inherently disclose any polymeric composition that is free flowing upon parenteral administration and at a temperature between 35 and 42°C as required in the amended claims.

In context, Rathi et al does not expressly or inherently teach any following limitations of amended claims 1-43: (a) an ABA or BAB block copolymer having a weight averaged molecular weight of between 1500 to 3099 Daltons, or (b) a polymeric composition when formed as an aqueous polymer solution remains a free flowing liquid upon parenteral administration to a warm blooded animal and at temperatures between 35 and 42°C. Rathi et al is directed to a different invention and does not anticipate amended claims 1-43 under 35 U.S.C. §102(b).

For the foregoing reasons, Applicants respectfully traverse and request withdrawal of the Examiner's rejection of claims 1-47 under 35 U.S.C. §102(b) over Rathi et al.

Applicants respectfully submit that amended Claims 1-47 are patentable under 35 U.S.C. §103(a) over Rathi et al.

An invention is unpatentable under 35 U.S.C. §103 for obviousness where "the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. §103(a). "The ultimate issue of obviousness turns on four factual determinations: (1) the scope and content of the prior art, (2) the level of ordinary skill in the art, (3) the differences

between the claimed invention and the prior art, and 94) objective indicia of nonobviousness." *Merck & Co. v. Teva Pharmaceuticals USA Inc.*, 73 USPQ.2d 1641 (Fed. Cir. 2005)(citing *Graham v. John Deere Co.*, 383 U.S; 1, 17-18 (1966)).

Applicants respectfully submit that amended Claims 1-43 are patentable under 35 U.S.C. §103(a) over Rathi et al. Claims 44-47 have been cancelled. One of the elements to establish a prima facie case of obviousness is that the combined references teach or suggest every claim limitation.

The Examiner seems to have incorrectly interpreted the claim term "upon administration" in the pending claims 1-43 of the present application and the teachings of Rathi et al. On pages 5 and 10 of the Office Action, the Examiner states:

> "Rathi [et al] discloses a water-soluble biodegradable ABA-type copolymer drug delivery system having a gelation temperature at or below the body temperature (abstract, column 4,lnes 57-65 and column 5, line 5), that is at body temperature the formulation is liquid and flowable meeting the limitation that the polymer solution is flowable at body temperature." (Office Action, page 5)
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> "The examiner disagrees because, just like the amended composition, the composition of Rathi is free flowing when administered." (Office Action, page 10).

Applicants incorporate by reference their detailed arguments above explaining the basis for interpreting the claim term "upon administration" to refer to the drug polymer solution when the drug enters the physiological system of a warm-blooded mammal and immediately thereafter.

Contrary to the Examiner's assertion, Rathi et al is directed to a polymeric composition possesses reverse thermal gelation properties and exists as a gel or semisolid at or below body temperature of a warm-blooded animal. (See, e.g, Column 6, lines 1-9 and 37-39.) Rathi et al describes these properties for its polymeric composition, for example, in the abstract:

> "At temperatures below the gelation temperature of the copolymer the composition is a liquid and at temperatures at or above the gelation temperature the composition is a gel or semi-solid. The gelation temperature is preferably at or below body temperature of a warm-blooded animal"."

Rathi et al further teaches that its polymeric solution is in the form of a "semisolid hydrogel (i.e., gels)" when exposed to body temperature. (E.g., Column 1, lines 16-23.) Rathi et al further teaches:

> "Therefore, the present invention is based on the discovery that ABA-type block copolymers, where the A-blocks are relatively hydrophobic poly(lactide-co-glycolide) and the B-block is a relatively hydrophilic polyethylene glycol, having a hydrophobic content of between about 50 to 83% by weight and an overall block copolymer molecular weight of between 3100 and 4500, exhibit water solubility at lower temperatures and undergo reverse thermal gelation at mammalian physiological body temperatures."

(Column 6, lines 31-39.) It is important to note that the present invention requires the polymeric composition to be free flowing during and immediately after parenteral administration to a warm-blooded animal and at temperatures between 35-42°C. Applicants respectfully submit that Rathi et al does not teach or suggest any polymeric compositions that remains free-flowing upon parenteral administration to a warm-blooded animal and at temperatures between 35 and 42°C as required by amended claims 1-43 of the present application.

In addition, the Examiner incorrectly states that Rathi et al discloses an ABA-type block copolymer which "gels at body temperature, which is 37°C (abstract and column 1, lines 19-21) and this means that between 35°C and 36.999°C, the ABA-type polymeric composition of Rathi is a liquid. In context, the cited portions of Rathi et al limitedly disclose that their compositions include "a select subset of such block copolymers" having a gelation temperature "at or below body temperature of a warm-blooded animal" which, "when the temperature is raised to about body temperature (typically 37°C for humans), spontaneously interacts to form solid hydrogels (i.e., gels)". (See Rathi et al, abstract and column 1, lines 15-23.) These cited portions of Rathi et al do not expressly or inherently disclose any polymeric composition that is free flowing upon parenteral administration and at a temperature between 35 and 42°C as required in the amended claims.

To reach a proper determination under 35 U.S.C. 103, the examiner must step backward in time and into the shoes worn by the hypothetical 'person of ordinary skill in the art' when the invention was unknown and just before it was made. MPEP §2142. In view of all factual information, the examiner must determine whether the claimed invention "as a whole" would have been obvious at that time to that person without the impermissible use of hindsight. MPEP §2142. A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. W.L. Gore & Associates, Inc. v. Garlock, 721 F.2d 1540 (Fed. Cir. 1983) MPEP §2141.02. In addition, a *prima facie* case of obviousness must establish some apparent reason why one would modify the expressly disclosed technology to achieve the composition expressly claimed in the present invention. *See KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1741

(citing *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006)('[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.') According to the Supreme Court, a proper case of *prima facie* obviousness must be articulated to a patent application by setting forth the reasoning and underlying rationale used to arrive at a legal conclusion of obviousness. *Id.*

In addition to the arguments above, Applicants respectfully submit that a prima facie case of obviousness of claims 1-43 over Rathi et al has not been provided. In responding to the Applicants' prior argument identifying the differences in required molecular weight range between Rathi et al (3100-4500) and the present invention 1500-3099), the Examiner provides the following conclusory statement:

> "Applicant has also argued the molecular weight range of 3100 to 4500 cannot anticipate a range of 1500 to 3099. The examiner agrees with applicant and that is why the rejection is made under 35 U.S.C. 103 and (0.999 = 99.9% of 3100 is 3096) rendering the claims obvious."

The foregoing conclusion suggests the use of impermissible hindsight. The Examiner has failed to provide any supporting basis to conclude that one of ordinary skill would have been motivated to modify the molecular weight range disclosed in Rathi et al to a new lower molecular weight range to form a polymeric composition that is free flowing upon parenteral administration to a warm-blooded animal.

Applicants respectfully submit that the one of ordinary skill in the art would not modify Rathi et al as asserted by the Examiner since Rathi et al teaches away from the claimed invention. Rathi et al is directed to a polymeric composition having block copolymers having a molecular weight of 3100-4500 Daltons which spontaneously forms a semisolid hydrogel (i.e., gel) upon administration to a warm-blooded animal. (See citations above.) Throughtout the specification (e.g., abstract; Column 1, lines 15-23; Column 4, lines 42-61; Column 5, lines 33-52; and Column 6, lines 31-41), Rathi et al emphasizes the importance of their invention is having a polymeric composition that has reverse thermal gelation properties and which exists as a gel upon administration to a warm-blooded animal but remains water soluble. One of ordinary skill in the art would have no motivation to ignore this primary teaching in Rathi et al and modify the key features without any technical basis to formulate a polymeric composition which is free-flowing upon administration to a warm blooded animal.

Applicants respectfully submit that dependent claims 2-3, 4-7, 9-11, 13-17, 19-22, 24-28, 30-33, 35-38, 40-43, 45 and 47 are in condition for allowance as it depends from an allowable independent claim.

For the foregoing reasons, Applicants respectfully traverse and request withdrawal of the Examiner's rejection of claims 1-47 under 35 U.S.C. §103 over Rathi et al.

Double Patenting Rejection

Claims 1-47 are rejected on the ground of nonstatutory obviousness-type double patenting as being allegedly unpatentable over claims 1-77 of U.S. Patent No. 6,201,072 to Rathi et al. (hereinafter "the '072 patent"). Claims 44-47 have been cancelled. The Examiner has asserted that Applicants' prior arguments distinguishing the '072 patent from the present invention of claims 1-47 are not persuasive "because the composition of 6,201,072 is also free flowing upon administration, that is when it is administered". The Examiner has also concluded that the '072 patent does not teach away from the present invention but provides no technical explanation for his conclusion.

The Examiner seems to have incorrectly interpreted the claim term "upon administration" in the pending claims 1-43 of the present application and the teachings of the '072 patent. Applicants incorporate by reference their detailed arguments above explaining the basis for interpreting the claim term "upon administration" to refer to the drug polymer solution when the drug enters the physiological system of a warm-blooded mammal and immediately thereafter. In the present invention of amended claims 1-43, the polymeric composition "remains a free flowing liquid upon parenteral administration to a warm blooded animal and at temperatures between 35 and 42°C" (emphasis added)

Since the analysis employed in an obviousness-type double patenting determination parallels the guidelines for a 35 U.S.C. §103(a) rejection, the factual inquires set forth in Graham v. John Deere Co., 383 U.S. 1 (1996) are applied. MPEP §804. Contrary to the Examiner's assertion, the '072 patent is not free flowing upon administration to a warm blooded animal as required by amended claims 1-43. The '072 patent is directed to a polymeric composition having reverse thermal gelation properties and that spontaneously forms a gel upon administration to a warm-blooded animal. The '072 patent describes these properties for its polymeric composition, for example, in the abstract:

> "At temperatures below the gelation temperature of the copolymer the composition is a liquid and at temperatures at or above the gelation temperature the composition is a gel or semi-solid. The composition may be administered to a warm-blooded animal...and is a gel at body temperature."

The '072 patent further teaches that its polymeric solution is in the form of a "semisolid hydrogel (i.e., gels)" when exposed to body temperature. (E.g., Column 1, lines 16-23.) Even when administered as a liquid, the '072 patent teaches that the '072 polymeric composition does not remain a free flowing liquid upon parenteral administration and at temperatures between 35-42° to a warm blooded animal as required by the present invention of amended claims 1-43. The '072 patent instead teaches:

> "This drug deliver liquid is then administered parenterally, topically, transdermally, transmucosally, inhaled, or inserted into a cavity such as by ocular, vaginal, transurethral, rectal, nasal, oral, buccal, pulmonary or aural administration to a patient, whereupon it will under go a reversible thermal gelation since body temperature will be above the gelation temperature."

(Column 9, lines 52-53.)

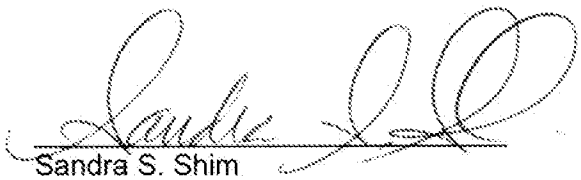
In addition, Applicants respectfully submit that one of ordinary skill in the art would not modify the '072 patent as suggested by the Examiner since the '072 patent teaches away from the claimed invention. The '072 patent is directed to a polymeric composition having block copolymers having a molecular weight between 2000 and 4990 Daltons which spontaneously forms a semisolid hydrogel (i.e., gel) upon administration to a warm-blooded animal. (See citations above.) Throughout the specification (e.g., abstract; Column 1, lines 2-34; Column 5, lines 5-21; Column 6, lines 11-19 and 26-41), the '072 patent emphasizes the importance of their invention is having a polymeric composition that has reverse thermal gelation properties and which exists as a gel upon administration to a warm-blooded animal but remains water soluble. One of ordinary skill in the art would have no motivation to ignore this primary teaching in the '072 patent and modify the key features without any technical basis to formulate a polymeric composition which is free-flowing upon administration to a warm blooded animal.

For the foregoing reasons, Applicants respectfully traverse and request withdrawal of the Examiner's double patenting rejection over the '072 patent.

In view of the foregoing arguments Applicants respectfully request that claims 1-43 of the present application be reconsidered. If a telephone interview would be of assistance

in advancing the prosecution of this application, Applicants' undersigned attorney invites the Examiner to telephone him at the telephone number provided below.

Respectfully submitted,



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